REMARKS/ARGUMENTS:

Claims 9, 10, 12-18, and 20-57 are canceled without prejudice. Claims 1-8 are amended. Support for the term "artificial intron" can be found, e.g., in paragraphs [0006], [0007], [0061]-[0063], [0079], Examples 8, 12 and in Figure 1 of U.S. Patent Publication No. 2004/025360. Support for the term "eukaryotic" can be found in paragraphs [0041], [0065] and in Example 9 of U.S. Patent Publication No. 2004/025360. Claims 1-8, 11, and 19 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

This invention relates to regulation of a gene function. (U.S. Patent Publication No. 2004/0253604).

CLAIM REJECTIONS UNDER 35 U.S.C. § 102:

Claims 1-3, 5, 7-12, 19, and 20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Mitchell, L. (U.S. Patent No. 6,013,487). This rejection is moot with respect to claims 9, 10, 12 and 20 due to the cancellation of these claims. Applicant respectfully traverses this rejection as to amended claims 1-3, 5, 7, 8, 11, and 19. Claims 1, as amended, is as follows:

> An isolated RNA comprising an artificial intron RNA that is released in a cell, thereby silencing the function of a target gene.

Applicant respectfully submits that Mitchell cannot anticipate or render claim 1 obvious, because Mitchell fails to teach or suggest "isolated RNA comprising an artificial intron RNA that is released in a cell, thereby silencing the function of a target gene."

Mitchell in Figures 1 and 2 teaches "trans-splicing" RNA (referred to as pre-therapeutic RNA). This RNA does not contain a 5'-splice donor site as is required for an intron. Since an intron must contain all four parts of the spliceosomal recognition site, including the 5'-splice donor site, the 3'-splice acceptor site, the branch site, and the poly-pyrimidine tract, Mitchell fails to teach or suggest an intron. Without the 5'-splice site, Mitchell's RNA is not an intron. In addition, as indicated in Figure 2 of Mitchell, the trans-splicing RNA is used to replace an intracellular cis-splicing intron for insertion of a foreign exon into the mRNA sequence, which is purposely different from the present invention. In the present invention, the RNA is used to silence a target gene, rather than to change the exon content of an mRNA. Furthermore, there is no teaching or suggestion in Mitchell that is related to the construction or utilization of an artificial intron RNA that is released in a cell for silencing a target gene.

In light of the foregoing, Applicant respectfully submits that Mitchell cannot anticipate or render claim 1 obvious, because Mitchell fails to teach or suggest each and every claim limitation. Claims 2, 3, 5, 11, and 19 depend from claim 1 and therefore, cannot be anticipated or rendered obvious for at least the same reasons as claim 1. Claims 7 and 8 similarly, require "isolated RNA comprising an artificial intron RNA that is released in a eukaryotic cell, thereby silencing the function of a target gene" and therefore, cannot be anticipated or rendered obvious for reasons discussed above. Withdrawal of this rejection is thus respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103:

Claims 1-12, 19, and 20 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mitchell, Krawczak et al. (Hum Genet 1992, Vol 90:41-54), and Zhuang et al. (PNAS 1989, Vol 86:2752-2756). This rejection is moot with respect to

claims 9, 10, 12, and 20 due to the cancellation of these claims. Applicant respectfully traverses this rejection as to amended claims 1-8, 11, and 19.

Claims 1-3, 5, 11, and 19 cannot be rendered obvious over Mitchell for the same reasons discussed above. Claims 4 and 6-8 depend from claim 1 and as such include all the limitations of claim 1, and therefore, cannot be rendered obvious over Mitchell for at least the same reasons discussed above. Krawczak and Zhang cannot remedy the defect of Mitchell and are not relied upon by the Office for such. Instead, the Office cites Krawczak for teaching a 5' splice donor site having a sequence that contains AAGTAAGT and Zhuang for teaching a preferred branch site sequence for mammalian mRNA splicing having the sequence UACUAAC.

Furthermore, there would not be any motivation to modify Mitchell since the modification of Mitchell would render Mitchell unsatisfactory for its intended purpose.

As discussed above, the trans-splicing RNA in Mitchell is used to replace an intracellular cis-splicing intron for insertion of a foreign exon into the mRNA sequence. In contrast, in the present invention, the RNA is used to silence a target gene, rather than to change the exon content of an mRNA. Also, as discussed above, the "trans-splicing" RNA (pre-therapeutic RNA) in Mitchell is not an intron. Adding a 5'-splice site and a branch site does not make the "trans-splicing" RNA of the Mitchell into a normal intron because the normal intron RNA goes through cis-splicing, **not** trans-splicing.

MPEP §2143.01(V) states,

> "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification."

In light of the foregoing, Applicant respectfully submits that the cited references either alone or in combination cannot render claims 1-8, 11, and 19

obvious, because the combination of references fails to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (310) 785-4600 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Date: June 10, 2008

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